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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,762	06/20/2002	Alexander James Bridges	A0000100-01-SMH	7601

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EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 06/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,762	BRIDGES ET AL.	
	Examiner	Art Unit	
	Shaojia A. Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *59,62,65-94 and 124* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59, 62, 65-94 and 124* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 11, 2005 has been entered.

This Office Action is in response to Applicant's request for continued examination (RCE) filed February 11, 2005, and amendment and response to the Final Office Action (mailed November 17, 2004), filed February 11, 2005 wherein claims 59, 62, 65-94 and 124 have been amended; claims 1-58, 60-61, 63-64, 95-123, and 125 are cancelled.

Currently, claims 59, 62, 65-94 and 124 are pending in this application and under examination on the merits.

Applicant's amendment that amends claims 59, 65-67, filed February 11, 2005 with respect to the rejection made under 35 U.S.C. 112 first paragraph for lack of scope of enablement of record stated in the Office Action dated November 17, 2004 has been fully considered and is found persuasive to remove or overcome the rejection since the claims have been limited to neuropathic pain. Therefore, the said rejection is withdrawn.

Applicant's amendment filed February 11, 2005 with respect to the rejection of claims 59-94 and 124 made under 35 U.S.C. 112 second paragraph for the use of the indefinite recitations, i.e., "a subject" of record stated in the Office Action dated November 17, 2004 has been fully considered and found persuasive to remove the rejection since the term "subject" has been removed from the claims and "mammal" has been recited. Therefore, the said rejection is withdrawn.

The following is the new ground(s) of rejection(s).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 59, 62, 65-94 and 124 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's amendment submitted February 11, 2005 with respect to amended claims 59, 62, 65-94 and 124 have been fully considered but is deemed to insert new matter into the claims.

The omission of an essential element of the invention, "chronic" pain in claims herein is deemed to raise new matter issue, i.e., an issue regarding whether the

inventor had possession of a broader, more generic invention. See, e.g., >PIN /NIP, Inc. v. Platte Chem. Co., 304 F.3d 1235, 1248, 64 USPQ2d 1344, 1353 (Fed. Cir. 2002). As noted in MPEP 2163, A claim that omits an element which applicant describes as an essential or critical feature of the invention originally disclosed does not comply with the written description requirement. See Gentry Gallery, 134 F.3d at 1480, 45 USPQ2d at 1503; In re Sus, 306 F.2d 494, 504, 134 USPQ 301, 309 (CCPA 1962).

In the instant case, the title of this application in the specification is directed to "METHOD FOR TREATING CHRONIC PAIN USING MEK INHIBITORS" (emphasis added). Thus, chronic pain or neuropathic chronic pain to be treated herein is considered to be an essential and critical element of the claimed invention, clearly supported by Applicant's specification as originally filed.

Moreover, Applicant's amendment with respect to new proviso limitation in claim 59 has been fully considered but is deemed to insert new matter into the claims since the specification as originally filed does not provide support for the proviso or negative limitation.

Any negative limitation or exclusionary proviso must have basis in the original disclosure. See Ex parte Grasselli, 231 USPQ 393 (Bd. App. 1983), aff 'd mem., 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement. See MPEP § 2163 - § 2163.07(b) for a discussion of the written description requirement of 35 U.S.C. 112, first paragraph.

Further, the specification as originally filed does not provide adequate support for the subgenus of compounds now claimed. As noted in MPEP 2163, "a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads", see *In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972).

Consequently, there is nothing within the instant specification which would lead the artisan in the field to believe that Applicant was in possession of the invention as it is now claimed. See *Vas-Cath Inc. v. Mahurkar*, 19 USPQ 2d 1111, CAFC 1991, see also *In re Winkhaus*, 188 USPQ 129, CCPA 1975.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 59-87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 59 recites "R_2 and R_3". There is insufficient antecedent basis for this limitation since there is not "R_2 and R_3" described in the structural formal (I)B and "W" and R_1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 59, 62, 65-66, 69, and 70 are rejected under 35 U.S.C. 102(b) as being anticipated by Connor et al. (EP 0 316 630 A, of record).

Connor et al. discloses that the active compounds of formula I which read on the instant compounds (see particularly page 5-6, e.g. Example 13 and 18at page 24-25), being cycloxygenase inhibitors, are useful in pharmaceutical compositions and methods for treating inflammation, arthritis, and pain (see abstract, page 4 lines 35-37, page 8 line 40-41, and claims 1-17).

Note that claim 62 herein recites the neuropathic pain is associated with inflammation, arthritis.

Further note that Connor et al. discloses that the effective amount of dexamethasone to be administered is in the range of 0.5 mg to 500 mg/kg/day or 0.5 mg to 50 mg/kg/day (see col.4 lines 15-17), which are within or overlapping with the effective amounts, 0.1-1000 mg/kg per day, preferably 1-300 mg/kg body weight, or daily dosages 10-5000 mg for an adult subject of normal weight, indicated in Applicant's specification (see page 74 line 29-31 of the specification).

Thus, Connor's method anticipates the claimed method, since Connor's method steps are same as the instant method steps, administering the same compound in the same amount to the same or similar patient population. See Ex parte Novitski, 26 USPQ 2d 1389, 1391 (Bd. Pat. App. & Int. 1993).

Thus, the disclosure of Connor et al. anticipates claims 59, 62, 65-66, 69, and 70.

Response to Argument

Applicant's arguments filed February 11, 2005 with respect to this rejection made under 35 U.S.C. 102(b) in the previous Office Action have been fully considered but are not deemed persuasive. These arguments are believed to be adequately addressed by the obvious rejection presented above.

Claims 59, 62, 65, and 70 are rejected under 35 U.S.C. 102(b) as being anticipated by Fujimura et al.: "HYDCOXAYIC ACID DEZIVATIVES" CHEMICAL ABSTRACTS + INDEXES, AMERICAN CHEMICAL SOCIETY. COLUM8US,US, vol. 70, no. 3 20 January 1966 (1969-01-20), or JP 42 024578 A or JP 42019583 B4 (TAKEDA CHEMICAL INDUSTRIAL LTD, 1967, of record).

Fujimura et al. discloses that the active compounds of formula I which read on the instant compounds (see particularly abstract), are useful as analgesics. Thus, these compounds are useful in pharmaceutical compositions and methods for treating neuropathic chronic pain (see abstract).

Fujimura et al. was silent regarding that the same compound herein is a MEK inhibitor, However, "a MEK inhibitor" is merely an inherent property of the known compound of Fujimura et al., or the mechanism of action of the known compound of Fujimura et al., adding nothing to the patentability of the claims, so long as the same compound is taught as analgesics.

Thus, the disclosure of FUJIMURA H et al. anticipates claims 59, 62, 65, and 70.

Response to Argument

Applicant's arguments filed February 11, 2005 with respect to this rejection made under 35 U.S.C. 102(b) in the previous Office Action have been fully considered but are not deemed persuasive as further discussed below.

Applicant asserts that analgesics cannot be used for treating chronic pain. Contrary to Applicant assertion, analgesics are well known to be used for treating neuropathic chronic pain according the Merck Manual discussed in the previous Office Action November 17, 2004.

Thus, the disclosure of FUJIMURA H et al. anticipates claims *59, 62, 65, and 70.*

Claims 59, 62, 65, and 69 are rejected under 35 U.S.C. 102(b) as being anticipated by Morkhort (of record).

Morkhort discloses that the active compounds therein which read on the instant compounds (see particularly abstract), are useful as analgesics. Thus, these compounds are useful in pharmaceutical compositions and methods for treating neuropathic chronic pain (see abstract).

Thus, the disclosure of Morkhort anticipates claims *59, 62, 65, and 69.*

Applicant's arguments filed February 11, 2005 with respect to that analgesics cannot be used for treating neuropathic chronic pain have been fully considered but are not deemed persuasive as discussed above.

Claims 59, 62, 65, 69 and 77 are rejected under 35 U.S.C. 102(b) as being anticipated by Hirano Hiroshi et al. (JP 42019583 B4 .TAKEDA CHEMICAL INDUSTRIAL LTD, 1967 of record).

Hirano Hiroshi et al. discloses that the active compounds therein which read on the instant compounds (see particularly abstract), are useful as analgesics. Thus, these compounds are useful in pharmaceutical compositions and methods for treating neuropathic chronic pain (see abstract).

Thus, the disclosure of Hirano Hiroshi et al. anticipates claims *59, 62, 65, 69 and 77*.

Applicant's arguments filed February 11, 2005 with respect to that analgesics cannot be used for treating chronic pain have been fully considered but are not deemed persuasive as discussed above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 59-94 and 124 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barrett et al. (WO 99/01421, PTO-1449 submitted May 16, 2003) in view of Walker et al. BRITISH JOURNAL OF CLINICAL PHARMACOLOGY, (1993 Nov)

36 (5) 417-25,) and Ma et al. (BRAIN RESEARCH, (1991 Dec 6) 566 (1-2) 95-102,) for the same reasons of record in the previous Office Action November 17, 2004.

Barrett et al. discloses that the active compounds of formula I which read on the instant compounds, have covered the instant compounds, or are structurally substantially similar to the instant compounds (see particularly Formula II, III and IIIa at page 5-6, and e.g. Example 212), being MEK inhibitors, are useful in pharmaceutical compositions and methods for treating inflammation (see abstract, page 1-3, and claims 1-34).

Barrett et al. do not expressly disclose the employment of the particular MEK inhibitors therein, in methods of treating neuropathic chronic pain.

Ma et al. teaches that pain (e.g., neuropathic pain) is known to be associated with MEK. See "abstract" in particular.

Walker et al. teaches that pain is well-known to be associated with inflammation. See "abstract" in particular.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular MEK inhibitors of Barrett et al. in methods of treating chronic pain.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ the particular MEK inhibitors of Barrett et al. in methods of treating chronic pain, because particular MEK inhibitors of Barrett et al. is known to be useful in methods of inflammation according to Barrett et al. It is also known that pain

e.g., neuropathic pain, is known to be associated with MEK according to Ma et al. Moreover, pain is well-known to be associated with inflammation.

Further, some of the instant compounds read on the compounds of Barrett et al. while other the instant compounds have been covered by the formula of Barrett et al., or are structurally substantially similar to. As noted in MPEP 2144, "If such a species or subgenus is structurally similar to that claimed, its disclosure may motivate one of ordinary skill in the art to choose the claimed species or subgenus from the genus, based on the reasonable expectation that structurally similar species usually have similar properties. See, e.g., Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also Deuel, 51 F.3d at 1558, 34 USPQ2d at 1214. The utility of such properties will normally provide some motivation to make the claimed species or subgenus. Id. Dillon, 919 F.2d at 697, 16 USPQ2d at 1904-05 (and cases cited therein). If the claimed invention and the structurally similar prior art species share any useful property, that will generally be sufficient to motivate an artisan of ordinary skill to make the claimed species, In fact, similar properties may normally be presumed when compounds are very close in structure. Dillon, 919 F.2d at 693, 696, 16 USPQ2d at 1901, 1904. See also In re Grabiak, 769 F.2d 729, 731, 226 USPQ 870, 871 (Fed. Cir. 1985) ("When chemical compounds have very close' structural similarities and similar utilities, without more a prima facie case may be made."). Thus, evidence of similar properties or evidence of any useful properties disclosed in the prior art that would be expected to be shared by the claimed invention weighs in favor of a conclusion that the claimed invention would have been obvious. Dillon, 919 F.2d at 697-98, 16 USPQ2d at 1905; In

re Wilder, 563 F.2d 457, 461, 195 USPQ 426, 430 (CCPA 1977); In re Linter, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972).

Therefore, one of ordinary skill in the art would have reasonably expected that the particular MEK inhibitors herein, would have beneficial therapeutic effects and usefulness in methods of treating pain caused by the particular disorders/diseases, e.g., neuropathic pain and inflammation, in patents suffering therefrom.

Thus the claimed invention as a whole is clearly prima facie obvious over the combined teachings of the prior art.

Response to Argument

Applicant's arguments filed February 11, 2005 with respect to this rejection made under 35 U.S.C. 103(a) in the previous Office Action have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as further discussed below as further discussed below.

Applicant also asserts that none of references provided the motivation to utilize the compounds in Barret for treating chronic pain. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 SPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

As discussed in the previous Office Action, one having ordinary skill in the art at the time the invention was made would have been motivated to employ the particular MEK inhibitors of Barrett et al. in methods of treating chronic pain, because particular MEK inhibitors of Barrett et al. is known to be useful in methods of inflammation

according to Barrett et al. It is also known that pain is well-known to be associated with inflammation. Note that Applicant admits in the specification, at page 2, lines 6-7, that the efficacy of anti-inflammatory agents toward chronic pain is weak. Nonetheless, whether the efficacy of anti-inflammatory agents toward chronic pain is weak or strong, is not at stake herein. Most importantly, the utility of anti-inflammatory agents for treating chronic pain is known in the art.

Therefore, motivation to combine the teachings of the prior art cited herein to make the present invention is seen. The claimed invention is clearly obvious in view of the prior art.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 59, 62, 68-94 and 124 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 24, 31, 33 of U.S. Patent No. 6,310,060.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to a method of treating a mammal suffering from a proliferative disease, diabetes, or cancer comprising administering the same compound as instantly claimed.

The claims herein are directed to in methods of treating neuropathic chronic pain. It is well-known that neuropathic chronic pain can be caused by late stage of proliferative disease or cancer, according to The Merck Manual of Diagnosis and Therapy (17th ED). Note that claim 62 herein recites the neuropathic pain is associated with diabetes.

Thus, the method in the instant application is seen to be obvious over the claims claims 24, 31, 33 of U.S. Patent No. 6,310,060.

Claims 59, 62, 68-94 and 124 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34-35, 41, 43 of U.S. Patent No. 6,506,798

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to a method of treating a mammal suffering from osteoarthritis, rheumatoid arthritis, diabetes or cancer comprising administering the same compound as instantly claimed.

The claims herein are directed to in methods of treating neuropathic chronic pain. It is well-known that neuropathic chronic pain can be caused by late stage of cancer,

according to The Merck Manual of Diagnosis and Therapy (17th ED). Note that claim 62 herein recites the neuropathic pain is associated with arthritis or diabetes.

Thus, the method in the instant application is seen to be obvious over the claims 34-35, 41, 43 of U.S. Patent No. 6,506,798.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Anna Jiang, Ph.D.
Primary Examiner
Art Unit 1617
May 20, 2005